

--In certain embodiments,  $X^1X^2X^3X^4X^5X^6$  is VRLHES (SEQ ID NO:6), or conservative substitutions thereof, and/or  $X^7X^8X^9X^{10}X^{11}X^{12}$  is LGQQVP (SEQ ID NO:7), or conservative substitutions thereof, and/or  $X^{14}X^{15}X^{16}$  is RFF (SEQ ID NO:8) or conservative substitutions thereof. In certain embodiments,  $X^{13}$  is not a cysteine and in particularly preferred embodiments,  $X^{13}$  is A.--

Delete the paragraphs at page 22, lines 12-31, and insert:

--In particularly preferred embodiments, mini-ARGP are represented by formula I (SEQ ID NO:9):



where  $X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}$ , and  $X^{16}$  are independently selected amino acids (including natural, synthetic, or modified amino acids); and  $n$  is zero or one. In certain embodiments, in each of the varied domains, one or more of the native residues can be preserved. Thus, for example,  $X^1X^2X^3X^4X^5X^6$  (SEQ ID NO:10) includes, but is not limited to  $VX^2X^3X^4X^5X^6$  (SEQ ID NO:11),  $X^1RX^3X^4X^5X^6$  (SEQ ID NO:12),  $X^1X^2LX^4X^5X^6$  (SEQ ID NO:13),  $X^1X^2X^3HX^5X^6$  (SEQ ID NO:14),  $X^1X^2X^3X^4X^5S$  (SEQ ID NO:15),  $VRX^3X^4X^5X^6$  (SEQ ID NO:16),  $VX^2LX^4X^5X^6$  (SEQ ID NO:17),  $VX^2X^3HX^5X^6$  (SEQ ID NO:18),  $VX^2X^3X^4EX^6$  (SEQ ID NO:19),  $VX^2X^3X^4X^5S$  (SEQ ID NO:20),  $X^1RLX^4X^5X^6$  (SEQ ID NO:21),  $X^1RX^3HX^5X^6$  (SEQ ID NO:22),  $X^1RX^3X^4EX^6$  (SEQ ID NO:23),  $X^1RX^3X^4X^5S$  (SEQ ID NO:24),  $X^1X^2LHX^5X^6$  (SEQ ID NO:25),  $X^1X^2LX^4X^5X^6$  (SEQ ID NO:26),  $X^1X^2LX^4EX^6$  (SEQ ID NO:27),  $X^1X^2LX^4X^5S$  (SEQ ID NO:28),  $X^1X^2X^3HEX^6$  (SEQ ID NO:29),  $X^1X^2X^3HX^5S$  (SEQ ID NO:30),  $X^1X^2X^3X^4ES$  (SEQ ID NO:31),  $VRLX^4X^5X^6$  (SEQ ID NO:32),  $VX^2LHX^5X^6$  (SEQ ID NO:33), VRLHES (SEQ ID NO:34) and the like. Similar permutations are available for  $X^7X^8X^9X^{10}X^{11}X^{12}$  (SEQ ID NO:35) (e.g. LGQQVP (SEQ ID NO:36),  $LX^8X^9X^{10}X^{11}X^{12}$  (SEQ ID NO:37),  $X^7GX^9X^{10}X^{11}X^{12}$  (SEQ ID NO:38),  $X^7X^8QX^{10}X^{11}X^{12}$  (SEQ ID NO:39),  $X^7X^8X^9QX^{11}X^{12}$  (SEQ ID NO:40),  $X^7X^8X^9X^{10}VX^{12}$  (SEQ ID NO:41),  $X^7X^8X^9X^{10}X^{11}P$  (SEQ ID NO:42),  $LGX^9X^{10}X^{11}X^{12}$  (SEQ ID NO:43),  $LX^8QX^{10}X^{11}X^{12}$  (SEQ ID NO:44),  $LX^8X^9QX^{11}X^{12}$  (SEQ ID NO:45),  $LX^8X^9X^{10}VX^{12}$  (SEQ ID NO:46),  $LX^8X^9X^{10}X^{11}P$  (SEQ ID NO:47),  $LGQX^{10}X^{11}X^{12}$  (SEQ ID NO:48), and the like).

Similarly, the "RFF" domain can be fully mutated or can retain one or more of the native residues. Thus, for example,  $X^{14}X^{15}X^{16}$  includes RFF (SEQ ID NO:8),  $R^{15}X^{15}X^{16}$  (SEQ ID NO:49),  $X^{14}FX^{16}$  (SEQ ID NO:50),  $X^{14}X^{15}F$ ,  $RFX^{16}$  (SEQ ID NO:51),  $RX^{15}F$  (SEQ ID NO:52),  $X^{15}FF$  (SEQ ID NO:53). In certain preferred embodiments,  $X^{13}$  is not cysteine.--

Delete the paragraph at page 30, lines 19-26, and insert:

--A feature of the subject non-peptide compounds is that they structurally mimic the active loop 3-D conformation when bound by the receptor. By active loop is meant residues 111-116 or Arg-Phe-Phe-Asn-Ala-Phe (SEQ ID NO:54) of the Agouti Related Protein. More specifically, the subject non-peptide compounds are characterized by substantially structurally mimicking the backbone phi angle of amino acid 113 in AGRP, *i.e.* Phe113 phi = -55.4°, and the  $U_1$ - $U_2$  interatomic distance (see structure below). As the subject compounds substantially structurally mimic the active loop, in 9 of 10 lowest energy structures calculated with distance geometry the following requirements should be met. --

Delete the paragraph at page 30, lines 19-26, and insert:

--Accordingly, one aspect of the invention pertains to a method of treating a disease state in mammals that is alleviated by treatment with a polypeptide having an amino acid sequence:  $CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}N AFC YCR_n$  (SEQ ID NO:9), wherein  $X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}$ , and  $n$  is 0 or 1, which method comprises administering to a mammal in need of such a treatment a therapeutically effective amount of the polypeptide, which can be administered, by way of illustration and not limitation, in a liquid formulations or a solid formulations, such as in the form of a pharmaceutically acceptable salt thereof. In one preferred embodiment, the polypeptide has the amino acid sequence: CVRLHESCLGQQVPCC DPAATCYCRFFNAFCYC (SEQ ID NO:3). In certain embodiments, such a disease state can be a wasting syndrome.--

In accordance with 37 CFR §1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) are provided in Appendix C.

### REMARKS

This amendment is provided in Response to the Notice to File Missing Parts of Nonprovisional Application. In response to the Notice, Applicant(s) request entry of this